

Application No.: 09/462,931
Amendment dated October 31, 2003
Reply to Office Action of June 6, 2003

Listing of the Claims

Claims 1-4 canceled.

Claim 5. (Previously presented):

A cell line producing the monoclonal antibody of claim 25.

Claims 6-7 canceled.

Claim 8 (Previously presented):

The immunoassay according to claim 26, wherein the non-competitive immunoassay is carried out in either a one-step or a two-step incubation procedure.

Claims 9-24 canceled.

Claim 25 (Currently amended):

A monoclonal antibody or recombinant antibody fragment which specifically binds a human gamma-carboxylated osteocalcin fragment, wherein said human gamma-carboxylated osteocalcin fragment is selected from the group consisting of

I) a fragment which ~~spans from amino acid in position 7 to amino acid in position 30~~ ^{24 aa} consists of amino acids 7 to 30 of the amino acid sequence set forth in SEQ ID NO:2 in which ~~all three~~ the glutamic acids in positions 17, 21 and 24 of said sequence are gamma-carboxylated, and

ii) a fragment which ~~spans from amino acid in position 6 to amino acid in position 30~~ ^{25 aa} consists of amino acids 6 to 30 of the amino acid sequence of SEQ ID NO:2 in which ~~all three~~ the glutamic acids in the positions 17, 21 and 24 of said sequence are

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gamma-carboxylated,

~~and wherein said monoclonal antibody or recombinant antibody fragment has the specificity to epitopes that have been identified on said gamma-carboxylated fragment of osteocalcin.~~

Claim 26 (Currently amended):

A non-competitive immunoassay for quantitative determination of a gamma-carboxylated osteocalcin fragment in a sample comprising contacting the sample with two monoclonal antibodies or recombinant antibody fragments which specifically bind said gamma-carboxylated osteocalcin fragment, measuring bound monoclonal antibody or recombinant antibody fragment, and comparing said amount with an amount measured in a sample having a known quantity of said gamma-carboxylated osteocalcin fragment, wherein said gamma-carboxylated osteocalcin fragment is selected from the group consisting of

i) a fragment which ~~spans from amino acid in position 7 to amino acid in position 30~~ consists of amino acids 7 to 30 of the amino acid sequence set forth in SEQ ID NO:2 in which ~~all three~~ the glutamic acids in positions 17, 21 and 24 of said sequence are gamma-carboxylated, and

ii) a fragment which ~~spans from amino acid in position 6 to amino acid in position 30~~ consists of amino acids 6 to 30 of the amino acid sequence of SEQ ID NO:2 in which ~~all three~~ the glutamic acids in the positions 17, 21 and 24 of said sequence are gamma-carboxylated, and

~~wherein said monoclonal antibody or recombinant antibody fragment has the specificity to epitopes that have been identified on said gamma-carboxylated fragment of osteocalcin.~~

Application No.: 09/462,931
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27. (New):

An immunoassay for determination of the presence of a gamma-carboxylated osteocalcin fragment in a sample comprising contacting the sample with a monoclonal antibody or recombinant antibody fragment which specifically binds said gamma-carboxylated osteocalcin fragment and determining the presence or absence of said antibody, wherein the presence of said antibody is indicative of the presence of said osteocalcin fragment, and wherein said gamma-carboxylated osteocalcin fragment is selected from the group consisting of

I) a fragment which consists of amino acids 7 to 30 of the amino acid sequence set forth in SEQ ID NO:2 in which the glutamic acids in positions 17, 21 and 24 of said sequence are gamma-carboxylated, and

ii) a fragment which consists of amino acids 6 to 30 of the amino acid sequence of SEQ ID NO:2 in which the glutamic acids in positions 17, 21 and 24 of said sequence are gamma-carboxylated.